

Immunogens of Pasteurella.

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Vet Microbiol (NETHERLANDS) Nov 1993, 37 (3-4) p353-68, ISSN
0378-1135 Journal Code: XBW

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

JOURNAL ANNOUNCEMENT: 9406

Subfile: INDEX MEDICUS

The family Pasteurellaceae Pohl contains Gram-negative, facultatively anaerobic and fermentative bacteria of the genera *Pasteurella*, *Haemophilus*, and *Actinobacillus*. Approximately 20 different species of the genus *Pasteurella* have been identified using phenotypic and genetic analyses. Of these species, *P. multocida* and *P. haemolytica* are the most prominent pathogens in domestic animals causing severe diseases and major economic losses in the cattle, swine, sheep, and poultry industries. Mechanisms of immunity to these bacteria have been difficult to determine, and efficacious vaccines have been a challenge to develop and evaluate.

Pasteurella multocida of serogroups A and D are mainly responsible for disease in North American poultry and pigs and to a lesser extent in cattle. Fowl cholera in chickens and turkeys is caused by various serotypes of *P. multocida* serogroup A and characterized by acute septicemia and fibrinous pneumonia or chronic fibrinopurulent inflammation of various tissues. Current biologicals in use are live *P. multocida* vaccines and bacterins. Potency tests for avian *P. multocida* biologicals are a bacterial colony count for vaccines and vaccination and challenge of birds for bacterins. Somatic antigens, particularly lipopolysaccharide (LPS), appear to be of major importance in immunity. In North American cattle, *P. multocida* serogroup A is associated mainly with bronchopneumonia (enzootic pneumonia) in young calves; however, it is occasionally isolated from fibrinous pleuropneumonia of feedlot cattle (shipping fever). Biologicals currently available are modified-live vaccines and bacterins. The potency test for vaccines is bacterial colony counts. The test for bacterin potency is vaccination and challenge of mice. Important immunogens have not been well characterized for *P. multocida* infection in cattle. In swine, *P. multocida* infection is sometimes associated with pneumonia; however, its major importance is in atrophic rhinitis. A protein toxin (dermonecrotic toxin), produced by toxigenic strains of *P. multocida* types A and D, and concurrent infection with *Bordetella bronchiseptica* appear to be the major factors in development of atrophic rhinitis. Currently available biologicals are bacterins and inactivated toxins (toxoids). The toxin appears to be the major immunogen for preventing atrophic rhinitis. There are, however, no standardized requirements for potency testing of *P. multocida* type D toxoid. Various serotypes of *P. haemolytica* biotype A are responsible for severe fibrinous pleuropneumonia of cattle and sheep, occasionally septicemia of lambs, and mastitis in ewes. Several serotypes of *P. haemolytica* biotype T are isolated from acute septicemia of lambs. The currently available *P. haemolytica* biologicals are modified-live vaccines, bacterins, bacterial surface extracts, and culture supernates that contain an exotoxin leukotoxin).(ABSTRACT TRUNCATED AT 400 WORDS)

(78 Refs.)

Efficacy of recombinant leukotoxin in protection against pneumonic challenge with live *Pasteurella haemolytica* A1.

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Infect Immun (UNITED STATES) Feb 1991, 59 (2) p587-91, ISSN 0019-9567

Journal Code: GO7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9104

Subfile: INDEX MEDICUS

The recombinant **leukotoxin** (rLKT) of the bacterium **Pasteurella haemolytica** A1 was examined for its ability to protect cattle from experimental challenge with logarithmic-phase *P. haemolytica*. Six different **vaccines** were utilized in the experiment: *P. haemolytica* culture supernatant, *P. haemolytica* culture supernatant enriched with rLKT, rLKT alone, *P. haemolytica* culture supernatant enriched with *Escherichia coli* supernatant not containing LKT, *E. coli* supernatant alone, and phosphate-buffered saline. rLKT alone showed no protective capacity against development of clinical signs of respiratory disease or against development of postmortem lung lesions after experimental challenge. It was, however, shown to enhance the efficacy of the culture supernatant **vaccine** and decrease clinical signs and pneumonic lesions. The complexity of protective immunity in this disease is emphasized in this study, and, although LKT is an important virulence factor of the organism, an immune response to LKT alone does not protect animals against disease.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: Bacterial Toxins--Immunology--IM; *Bacterial Vaccines --Immunology--IM; *Exotoxins--Immunology--IM; * **Pasteurella** --Immunology --IM; *Pasteurellosis, Pneumonic--Prevention and Control--PC; Cattle; Recombinant Proteins--Immunology--IM

CAS Registry No.: 0 (leukotoxin); 0 (Bacterial Toxins); 0 (Bacterial Vaccines); 0 (Exotoxins); 0 (Recombinant Proteins)

Identification of RTX toxin target cell specificity domains by use of hybrid genes.

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Infect Immun (UNITED STATES) Nov 1991, 59 (11) p4212-20, ISSN 0019-9567 Journal Code: G07

Contract/Grant No.: AI20323, AI, NIAID

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9202

Subfile: INDEX MEDICUS

The *Escherichia coli* hemolysin (HlyA) and *Pasteurella haemolytica* leukotoxin (LktA) are cytolytic toxins encoded by genes belonging to the recently described RTX gene family. These cytotoxins are, respectively, 1,023 and 953 amino acids in length and are encoded by genes within identically organized operons. They share 45% amino acid sequence identities but differ in their target cell specificities. In vitro-derived recombinant hybrid genes between hlyA and lktA were constructed by using restriction endonuclease sites created by oligonucleotide site-directed mutagenesis. The cytolytic activity of hybrid proteins was investigated using as targets sheep erythrocytes and two cultured cell lines from different species (BL3, bovine leukemia-derived B lymphocytes; and Raji, human B-cell lymphoma cells). HlyA is cytolytic to all three cell types. LktA lyses only BL3 cells. Among the hybrid proteins displaying cytolytic activity, the striking finding is that the hemolytic activity of several LktA-HlyA hybrids was independent of any cytolytic activity against either cultured cell species. The hemolytic activity was associated with the HlyA region between amino acids 564 and 739. Structures that are critical for HlyA cytolytic activity against BL3 or Raji cells were destroyed when LktA-HlyA and HlyA-LktA hybrids were made, respectively, at amino acid positions 564 and 739 of HlyA. In contrast to HlyA, which lysed the two different cultured cell lines with equal efficiency, Lkt-HlyA hybrids possessing the amino-terminal 169 residues of LktA lysed BL3 cells more efficiently than Raji cells. This suggests that a significant but not exclusive element of the LktA ruminant cell specificity resides in the amino-terminal one-fifth of the protein. A molecular model of the functional domains of HlyA and LktA is presented.

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